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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/844,517	04/27/2001	Erich Hoffmann	2427/1G772-US1	9063

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EXAMINER
HILL, MYRON G

ART UNIT	PAPER NUMBER
1648	15

DATE MAILED: 08/09/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/844,517	HOFFMANN, ERICH	
	Examin r	Art Unit	
	Myron G. Hill	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 May 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1- 41* is/are pending in the application.

4a) Of the above claim(s) *1- 14, 33- 38, 40 ,and 41* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15- 32, and 39* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892) /
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 4, 5, 8 /
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

Applicant's election with traverse of Group II in Paper No. 14 is acknowledged. The traversal is on the ground(s) that Groups II and IV are in the same class, that II and III are related, and that I is used in II. This is not found persuasive because Group IV is not in the same subclass and therefore requires a different search and there is no direct link between the two Groups, and Group III is not limited to viruses produced by claim 29 and requires additional search for the method. Invention I could be rejoined if the plasmids were the same scope (claims are drawn to an expression plasmid with no insert and it is not clear what the plasmid "expresses" in claim 1). Group I is not limited to the plasmids used in Group II.

The requirement for Groups III and IV are still deemed proper and is therefore made FINAL.

Claims 1- 14, 33- 38, 40, and 41 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 15- 32, and 39 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term "autonomous" in claim 15 is not clear as to what it specifies beyond viral genomic segment or if it can act by itself. The word "minimum" in claim 15 is a relative term that lacks a comparative basis and therefore it is not clear what is meant by minimum. It is not clear what the minimum set of plasmids comprising genomic segments required for generation of infectious negative stranded viruses is. It is also not clear in line 3 of claim 15 if the cloned viral cDNA of line 2 and if said cloned viral cDNA corresponds to one autonomous viral genomic segment. The "are" in line 6 of claim 15 refers to an inserted DNA sequence or something more? It is not clear what "having a map selected from" in claims 23, and 24 means.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 15- 32, and 39 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for production of influenza viruses, does not reasonably provide enablement for the full range of negative stranded viruses. The specification does not enable any person skilled in the art to which it pertains, or with

which it is most nearly connected, to use the invention commensurate in scope with these claims.

The specification teaches a method to make an influenza virus using a plasmid expression system that makes both vRNA and mRNA from the same plasmid using POLI and POLII. The rescue of influenza from cloned viral RNA expressed from plasmids that express vRNA (8 plasmids, one for each genomic segment) and separate plasmids that express support proteins has been done by Neumann (1999, in IDS).

The POLI and POLII expression systems work in the nucleus of the cell and this is where influenza viruses normally replicate. This system with "two promoter expression of one DNA sequence in cassette" plasmids works for influenza because all the needed support proteins are expressed from the plasmids as mRNA (and able to be made into proteins and used for encapsidation and polymerase activity). It is not clear that this strategy will work for other negative stranded viruses especially nonsegmented viruses that at most will be able to make mRNA from the first gene of the genome, and ones that replicate in the cytoplasm, not the nucleus. For nonsegmented viruses additional plasmids to supply support proteins will be needed and these would not have to be supplied by the special POLI POLII expression plasmid. It seems that "minimum" plasmid system relates to one plasmid for each segment of infuenza virus and no support provided except for the plasmids. No examples have been shown that demonstrate a successful rescue of a nonsegmented virus that replicates in the cytoplasm with a minimum number of plasmids. Page 29, lines 16- 24 defines the

"minimum plasmid-based" system as the total number of plasmids will not exceed the total number of gene segments from the source virus.

Due to the large quantity of experimentation necessary to rescue any negative stranded virus with the minimum plasmid based system as defined in the specification, the lack of direction/guidance presented in the specification regarding non-segmented negative stranded viruses and the well known fact in the art that these non-segmented negative stranded viruses require support and encapsidation to be infectious and make virions, the absence of working examples directed to non-segmented negative stranded viruses, the complex nature of the invention, and the breadth of the claims which fail to limit the claims to influenza, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claims 23 and 24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. It is apparent specific plasmids are required to practice the claimed invention. As such they must be readily available or obtainable by a repeatable method set forth in the specification, or otherwise known and readily available to the public. If it is not so obtainable or available, the requirements of 35 U.S.C. 112, first paragraph, may be satisfied by an enabling deposit of the plasmids. Therefore, a deposit at a recognized depository may be made for enablement purposes.

If a deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicants, or statement by an attorney of record over his or her signature and registration number, stating that the instant invention will be irrevocably and without restriction released to the public upon the issuance of a patent, would satisfy the deposit requirement made herein. If a deposit has not been made under the Budapest Treaty, then in order to certify that the deposit meets the criteria set forth in 37 CFR 1.801-1.809 and MPEP 2402-2411.05, Applicant may provide assurance of compliance by affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number showing that:

(a) during the pendency of the application, access to the invention will be afforded to the Commissioner upon request;

(b) all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;

(c) the deposit will be maintained in a public depository for a period of 30 years. Or 5 years after the last request for the enforceable life of the patent, whichever is longer;

(d) a test of the viability of the biological material at the time of deposit (see CFR 1.807); and

(e) the deposit will be replaced if it should ever become inviable.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 15- 32, and 39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hoffmann (1997, from IDS) and Neumann (PNAS, 1999 in IDS).

Hoffmann teaches a POLI-POLII plasmid expression system that can be used to express vRNA and mRNA (pages 112- 126). Hoffmann teaches that this system can be used to make RNA with precise ends to make vRNA or cRNA with the POLI promoter terminator and this is inserted between a POLII promoter and polyA signal which can be used to drive mRNA synthesis. Hoffman teaches that only genomic segments with correct ends can be packaged and shows that CAT activity can be detected after passage demonstrating that the segments are packaged and can be translated.

Hoffmann does not teach tranfection of all eight plasmids encoding a viral segments.

Neumann (PNAS, 1999 in IDS) teaches the rescue of infectious influenza virus with 12 plasmids (8 expressing vRNA segments and 4 expressing mRNA for support proteins). Neumann also teaches that transfection with 8 plasmids expressing vRNA segments and 8 expressing mRNA for all the proteins was more efficient. Neumann also teaches this system is efficient, does not require helper viruses, and useful for making vaccines and gene therapy vectors (abstract).

The level of skill in the art of inflenza reverse genetics is very high and the viruses in general are very well characterized.

Knowing the plasmid of Hoffmann can produce vRNA that can be incorporated into virions (making authentic vRNA segments) and mRNA to make support proteins from the same plasmid, and that tranfection with all support plasmids is more effient as taught by Neumann, one would have been motivated to use the plasmids of Hoffmann to make the rescue system of Neumann more efficient because it would require making fewer plasmids (a "minimum" number) as well as the other advantages taught by Neumann.

Thus, it would be *prima facie* obvious to make recombinant influenza viruses with the plasmid of Hoffmann.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Myron G. Hill whose telephone number is 703-308-4521. The examiner can normally be reached on 9am-6pm Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4247. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Myron G. Hill
Patent Examiner
August 8, 2002

MARY E. MOSHER
PRIMARY EXAMINER
GROUP 1800

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